

The Integration of Multiple Negative Feedback Regulators Directs Diverse NF- κ B Signaling Dynamics

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The paradigm for transmission of information in mammalian cells is a stimulus-induced cascade of signaling events culminating in the expression or activation of downstream components. Signal transduction is seldom linear and the redundancies inherent in the network through combinatorial complexity complicate our understanding of the signaling process. The Nuclear Factor (NF) κ B signaling pathway is central to a host of physiological responses and is controlled through a robust, non-linear network of interactions that responds to both homeostatic and stimulus-dependent controls. Through computational and biochemical studies, we have elucidated the interactions between multiple negative feedback regulators that enable stimulus and temporal-specific control of NF- κ B responses.